MEMORANDUM

To: Bill Patterson
From: Burton Craige, Legal Affairs Counsel, North Carolina Advocates for Justice
Date: March 22, 2012
Subject: Pharmaceutical liability bill – the illusory "fraud exception"

Introduction

Subsection (b)(2) of the pharmaceutical bill provides an apparent exception to immunity if the claimant proves that the drug manufacturer "Intentionally, and in violation of applicable regulations *as determined by final agency action*, withheld from or misrepresented to the United States Food and Drug Administration information material to the approval or maintaining of approval of the drug, and such information is relevant to the harm which the claimant allegedly suffered."

This memorandum responds to the following question in your March 12 email: "In what cases, if any, has the FDA taken 'final agency action' with regard to allegations of fraud by manufacturers?"

Summary

The FDA never makes a determination by "final agency action" that a drug manufacturer or seller has provided misleading information or withheld information related to receiving or maintaining drug approval. The FDA's general approach to fraudulent drug applications is to issue warning letters. When there is an ongoing pattern of fraud, the FDA invokes an Application Integrity Policy to suspend review of the applications. Neither response is a final agency action.

The FDA has broad authority to respond to fraudulent drug applications

When the FDA approves a drug, it relies on information provided by the drug companies. Drug companies that submit false or misleading information to the FDA undermine the integrity of the approval process and jeopardize the public's safety. Federal law prohibits false or fraudulent statements of material fact to federal agencies.[i] More specifically, the Food, Drug, and Cosmetic Act prohibits entities and individuals from submitting false or misleading clinical trial information to the FDA or failing to submit required post-approval information such as adverse side effects that come to light after a drug has been approved.[ii]

The FDA has three types of actions with which to respond to false or misleading drug applications: (1) advisory actions, (2) judicial actions, and (3) administrative actions. The FDA's advisory actions include issuing warning letters and providing informal recommendations to the industry. Judicial actions include pursuing criminal prosecutions and seizing unsafe products. Administrative actions include denying drug approval, withdrawing drug approval, and prohibiting submission of any future FDA drug applications ("debarring").

The FDA does not take "final agency action" in response to fraud.

"Final agency action" has a specific legal meaning and refers to a small subset of administrative actions that determine a party's rights or obligations as a result of the final stage of the agency's decision-making process.[iii] Final agency action does not include advisory actions, judicial actions, or agency decisions and conclusions made in the course of the agency's investigations. Very few of the FDA's possible responses to fraud are final agency actions.

The FDA's primary final agency actions are recalling products, debarring entities and individuals, issuing civil fines, and denying or withdrawing drug approval. However, the FDA has not taken such actions against a drug company in response to a fraudulent or misleading drug application.

- The FDA is not authorized to recall drugs based on fraud.[iv]
- The FDA has never debarred a drug company.[v]
- A review of the FDA's Enforcement Reports for the last eight years revealed no "final agency actions" against drug companies for fraud.[vi]
- Penalties against drug companies in settlements and plea agreements are the result of judicial actions, not final agency actions.

The FDA's policy is to respond to fraudulent drug applications by issuing warnings and suspending review of applications.

When the FDA has conducted an investigation of a drug company and found irregularities in the data, the FDA's most common response is to send a warning letter. Each year, the FDA issues multiple warning letters to drug companies for problems related to the integrity and completeness of drug applications.[vii] Typical warning letters describe the drug companies' failure to monitor clinical investigators, failure to ensure the accuracy and integrity of data, and failure to submit required reports. Warning Letters are not "final agency actions."[viii] Warning letters inform the drug company of the results of the FDA's investigation and provide notice that the FDA can take additional action if the drug company does not cooperate to improve the integrity of the data.

Some drug companies persist in submitting misleading information even after repeated warnings. The FDA has stated that its "general approach regarding applicants that seek to subvert the agency's review and approval processes" for drug applications is to invoke the Application Integrity Policy, also called the "Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities; Final Policy."[ix] When the FDA invokes the Application Integrity Policy, it suspends scientific review of the drug applications until the FDA is confident that the applications are trustworthy. The Application Integrity Policy generally requires the offending drug company to hire outside auditors, develop integrity assurance procedures, and demonstrate the integrity of the data. The FDA invokes the Application Integrity Policy when there is a pattern or practice of wrongful conduct that raises serious questions about the reliability of material information submitted to the FDA.[x] The FDA has invoked the policy twelve times.[xi]

Even in the most egregious cases of fraud, the FDA has not taken final agency action.

Every few years there is a new, shocking example of a drug company that commits scientific fraud, dupes the FDA, and makes millions of dollars selling dangerous drugs to the unsuspecting public.[xii] Often, dangerous drugs remain on the market for years with fraudulently obtained FDA approval. Time after time, an individual clinical investigator takes the fall, and the drug company receives a warning. The FDA does not make a determination of fraud by final agency action against the drug company.

Conclusion

This bill protects drug companies that submit fraudulent drug applications that are never discovered. This bill protects drug companies when there is evidence of fraud in congressional hearings, warning letters, and FDA investigations. This bill protects drug companies that have been found guilty of fraud in court orders, settlements, and plea agreements. This bill does not protect North Carolinians.

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[i] 18 USC 1001(a).
[ii] 21 USC 331; 21 CFR 314.80; 21 CFR 314.81.
[iii] *Bennett v. Spear*, 520 U.S. 154, 177-178 (1997) citing *Chicago & Southern Airlines, Inc. v. Waterman S.S. Corp.,* 333 U.S. 201, 113 (1948).
[iv] Congressional Research Service. *The FDA's Authority to Recall Products*. By Vanessa K. Burrows. (2010), available at http://www.nationalaglawcenter.org/assets/crs/RL34167.pdf
[v] FDA, Inspections, Compliance, Enforcement, and Criminal Investigations. *FDA Debarment List (Drug Applications)*, (2012), available at http://www.fda.gov/ICECI/EnforcementActions/FDADebarmentList/default.htm
[vi] *See* FDA, *Enforcement Reports*, (2012), available at http://www.fda.gov/Safety/Recalls/EnforcementReports/default.htm
[vii] FDA, Inspections, Compliance, Enforcement, and Criminal Investigations, *Warning Letters,* (2012), available at http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/default.htm
[viii] *Holistic Candlers and Consumers Ass'n, et al. v. FDA,* 770 F. Supp. 2d 156 (D.D.C. 2011)
[ix]FDA, *Application Integrity Policy,* (2009), available at http:// www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrity Policy/ucm134741.htm
[x] Id.
[xi] FDA, Inspections, Compliance, Enforcement, and Criminal Investigations, *Application Integrity Policy List,* (2011), available at http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/ucm134453.htm
[xii] *See e.g.,* media coverage of fraudulent drug applications submitted by Ranbaxy Laboratories Ltd. (2012), Metabolife Inc. (2008), and Aventis Pharmaceuticals (2007).